REMARKS/ARGUMENTS

Status of the Claims

Claims 1-5, 11-14, 17, 18, 23, 25-27, and 29-31 stand rejected.

Reexamination and reconsideration of the application are respectfully requested in view of the following remarks.

The Rejection of the Claims Under 35 U.S.C. § 103(a) Should Be Withdrawn

Claims 1-5, 11-14, 17, 18, 23, 25-27, and 29-31 remain rejected under 35 U.S.C. § 103(a) as being unpatentable over Klimyuk *et al.* (WO 02/088369) in view of Hooykaas *et al.* (WO 01/89283) for the reasons of record in the Office Actions mailed April 15, 2008 and January 5, 2009. This rejection is respectfully traversed.

Applicants note that the Examiner seems to have disregarded most of Applicants' arguments on non-obviousness as set forth in their previous response filed July 6, 2009. In any event, the Examiner does not provide in the Office Action detailed comments on any of Applicants' arguments.

As stated on page 4 of the Office Action, the Examiner has taken the position that:

> The only difference between Hooykaas et al and the present invention appears to be that Hooykaas et al directly introduce the fusion protein versus the present invention wherein a vector encoding the fusion protein is introduced.

Applicants respectfully disagree with this position and earnestly believe that the Examiner has misunderstood their claimed invention. Thus, Applicants provide below an explanation of their claimed invention and a discussion of why their invention is not obvious in view of the cited combination of documents.

For the present invention, the method of claim 1 comprises two steps, namely a step (a) of providing a plant organism and a step (b) of causing expression by delivering a polypeptide to the plant organism. The plant provided in step (a) comprises a heterologous nucleic acid that is the target of the recombinase or intetgrase delivered with the polypeptide of step (b) as well as for the protein expressed from the nucleic acid.

In Hooykaas *et al.*, a plant is provided (step (a)) that contains a heterologous nucleic acid that is the target for the cre recombinase delivered as a fusion with a part of VirE by the transfer system of Hooykaas et al. (step (b)). See, the figure in Hooykaas *et al.*

From the Examiner's statement cited above, it appears that the Examiner identifies the fusion of VirE and cre recombinase delivered in step (b) of Hooykaas *et al.* with the protein encoded, in the present invention, by the heterologous nucleic acid of step (a). Thus, the examiner confuses the first and second steps and, as well as the target (nucleic acid) of the recombinase and the targeting recombinase acting on the target nucleic acid.

If the delivery of the VirE-cre-fusion of Hooykaas *et al.* is construed to correspond to step (a) of claim 1 (with the only difference that a protein is delivered by the method of Hooykaas *et al.* and a nucleic acid vector as used in the methods of the instant invention), then the method of Hooykaas *et al.* has no step corresponding to step (b) of claim 1.

Moreover, even if Hooykaas *et al.* delivered the VirE-cre-fusion in the form of a nucleic acid encoding the VirE-cre-fusion, no embodiment of claim 1 would be obtained, since such a nucleic acid would not fulfill item (ii) of claim 1, *i.e.*, being capable of causing its own expression from the heterologous nucleic acid, as Hooykaas *et al.* contains no suggestion to this end.

In summary, if the delivery of the fusion protein by the transfer system of Hooykaas *et al.* is identified with step (a) of claim 1, claim 1 differs from Hooykaas *et al.* by

- step (b) of claim 1 and

- in that Hooykaas *et al.* does not suggest to use a nucleic acid encoding the recombinase, wherein the nucleic acid is the target for the recombination activity of the recombinase.

Moreover, such a construction would require the delivery of the fusion protein into cells as a nucleic acid, which is in contradiction with the very teaching of Hooykaas *et al.*, which intends to translocate polypeptides, as opposed to nucleic acids, into cells.

The discussion above shows that the construction of Hooykaas *et al.* apparently used by the Examiner differs fundamentally from the present invention, and that the alleged "only difference" found by the Examiner is in fact not the only difference Applicants' claimed invention and the disclosure of Hooykaas *et al.*

If, alternatively, the provision of the target cells of Hooykaas *et al.* (shown at the top of the figure of Hooykaas *et al.*) is identified with step (a) of claim 1, and the delivery of the VirE-cre-fusion of Hooykaas *et al.* is identified with step (b) of claim 1, claim 1 differs from Hooykaas *et al.* in that Hooykaas *et al.* does not disclose:

> providing a multi-cellular plant organism or part thereof, whereby cells of said multi-cellular plant organism or said part contain a heterologous nucleic acid encoding a protein, wherein said protein comprises the protein portion of item (i) of claim 1 and a segment according to item (ii) of claim 1.

It is not reasonable to assume that the nptII resistance gene expressed by Hooykaas *et al.* by the action of cre is capable of leaving a cell and entering other cells as required by item (i) of claim 1. Notably, Hooykaas *et al.* does not disclose a plant containing a heterologous nucleic acid encoding a protein capable of causing expression of said protein (item (ii) of claim 1), *i.e.*, its own expression.

The above discussion shows that the Examiner's assumption on the only difference between claim 1 and Hooykaas *et al.* is clearly incorrect.

Klimyuk *et al.* does not disclose a link between Hooykaas *et al.* and claims 1 and 27. Notably, Klimyuk *et al.* does not disclose expression, from a heterologous nucleic acid, of a fusion protein as defined in items (i) and (ii) of claim 1 that causes its own expression from the heterologous nucleic acid. As Applicants explained in their previous response, a viral movement protein and cre may be expressed according to Klimyuk *et al.*, but they are separate proteins and they are not expressed from the same type of heterologous nucleic acid, but from different nucleic acids. Therefore, the function of these proteins in Klimyuk *et al.* is unrelated to that used in the present invention. Moreover, even when combined with Hooykaas *et al.*, this combination of documents fails to render obvious the present invention.

In the present invention, the protein is capable of causing its own expression. The features (i) and (ii) provide the method with the advantage that expression may be induced in only a small number of cells by the external application of a signal that causes the expression of part (b) of claim 1. The expressed protein can then spread to cells that have not been reached by the external signal and cause expression of said protein in such cells. In this way, the externally applied signal is amplified and spread in plant tissue, allowing control of the plant in many more cells or tissues than could be reached by the external signal. Klimyuk *et al.* contains no suggestion to the use of a protein having, at the same time, the functions of features (i) and (ii) above. Instead, Klimyuk *et al.* uses viral vectors that may express a viral movement protein or coat protein that allow movement of the viral vector in plant tissue. The movement or coat protein does not, however, cause its own expression and does not have any of the activities recited in part (ii) of amended claim 1.

In summary, one of skill in the art would not find that the subject matter encompassed by the pending claims is obvious in view of the combination of Klimyuk *et al.* and Hooykaas *et al.* More importantly, even if the skilled person had combined the teaching of Klimyuk *et al.* and Hooykaas *et al.* this combination fails to provide all of the elements of the pending claims. Therefore, the Examiner has failed to raise a *prima facie* case of obviousness under 35 U.S.C. § 103(a).

In view of the above remarks, it is submitted that the rejection of the claims under 35 U.S.C. § 103(a) should be withdrawn.

Status of the Claims of Co-Pending Application No. 10/535,766

The pending claims of co-pending Application No. 10/535,766 (371(c) date June 22, 2005) are drawn to a method of controlling a genetically modified plant or plant cells and plants and compositions used in this method. The method comprises the steps of providing a genetically-modified plant or plant cells, wherein the plant or plant cells contain a heterologous nucleic acid encoding a first polypeptide containing or consisting of a first fragment of a protein, introducing a second polypeptide into cells of the genetically-modified plant or plant cells, wherein the second polypeptide containing a second fragment of the protein and a peptide sequence enabling the introduction of the second polypeptide into cells of the genetically-modified plant or plant cells, whereby the first fragment and the second fragment jointly generate a predetermined function of the protein only when jointly present. Claims 1, 3, 5, 7-9, 21, 23-28, and 31 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Klimyuk *et al.* (WO 02/088369) in view of Hooykaas *et al.* (WO 01/89283) and further in view of Xu *et al.* (WO 00/71701).

Status of the Claims of Co-Pending Application No. 10/535,780

The pending claims of co-pending Application No. 10/535,780 (371(c) date June 22, 2005) are drawn to a method of controlling a controlling a genetically-modified plant and plants and compositions used in this method. The method comprises the steps of providing a genetically-modified plant, whereby cells of said genetically-modified plant contain a heterologous nucleic acid and whereby the genetically-modified plant is inactive with regard to a cellular process of interest, and switching on the cellular process of interest by directly introducing a polypeptide from a cell-free composition into cells containing the heterologous nucleic acid, wherein the polypeptide and said heterologous nucleic acid are mutually adapted such that the polypeptide is capable of switching on the cellular process of interest. Claims 1, 6-

8, 11, 13-17, 25, 26, and 31 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Hooykaas *et al.* (WO 01/89283). Claims 1, 2, 6-8, 11, 13-22, 25-28 and 31 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Klimyuk *et al.* (WO 02/088369) in view of Hooykaas *et al.* (WO 01/89283) and further in view of Xu *et al.* (WO 00/71701).

CONCLUSIONS

In view of the above remarks, Applicants submit that the rejections of the claims under 35 U.S.C. § 103(a) are overcome. Applicants respectfully submit that this application is now in condition for allowance. Early notice to this effect is solicited.

If in the opinion of the Examiner a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefor (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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